



## SEQUENCE LISTING

<110> Pepinsky, Blake  
Runkel, Laura  
Brickelmaier, Margot  
Whitty, Adrian  
Hochman, Paula

<120> Polymer Conjugates of Interferon Beta-1a and Uses

<130> BII-008.02

<140> 10/802,540

<141> 2004-03-16

<150> 09/832,658

<151> 2001-04-11

<150> PCT/US99/24201

<151> 1999-10-15

<150> 60/104,572

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Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
 35 40 45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
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 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
 100 105 110  
 Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125  
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
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 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
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 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
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 Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
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 Thr Gly Tyr Leu Arg Asn  
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 Ala Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
 35 40 45  
 Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
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Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
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 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
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 Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
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 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Arg Ile Asn Arg Leu  
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 Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
             50                            55                            60  
 Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
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 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
                             85                            90                            95  
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
                             100                            105                            110  
 Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
             115                            120                            125  
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
             130                            135                            140  
 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Arg Ile Asn Arg Leu  
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 Thr Gly Tyr Leu Arg Asn  
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 Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
 65 70 75 80  
 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
 85 90 95  
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
 100 105 110  
 Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125  
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
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 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Arg Ile Asn Arg Leu  
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 Thr Gly Tyr Leu Arg Asn  
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 Asn Ile Ala Ser Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
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Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
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His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
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Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
115 120 125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
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Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Arg Ile Asn Arg Leu  
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Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
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Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
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Asn Ile Phe Ala Ile Phe Ala Ala Ala Ser Ser Ser Thr Gly Trp Asn  
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Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
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His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
100 105 110

Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
115 120 125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
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Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Arg Ile Asn Arg Leu  
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Thr Gly Tyr Leu Arg Asn  
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<210> 33

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&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 33

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          20           25           30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
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Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
          50           55           60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
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Ala Ser Ile Val Ala Ala Leu Leu Ser Asn Val Tyr His Gln Ile Asn
          85           90           95

His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
          100          105          110

Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
          115          120          125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
          130          135          140

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Arg Ile Asn Arg Leu
          145          150          155          160

Thr Gly Tyr Leu Arg Asn .
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&lt;210&gt; 34

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&lt;212&gt; PRT

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&lt;400&gt; 34

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Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
 1           5           10           15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
          20           25           30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
          35           40           45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
          50           55           60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
65           70           75           80

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 1           5           10           15

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      20           25           30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
      35           40           45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
      50           55           60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
65           70           75           80

Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
      85           90           95

His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Ala Ala Thr
      100          105          110

Ala Gly Ala Ala Met Ser Ala Leu His Leu Lys Arg Tyr Tyr Gly Arg
      115          120          125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
      130          135          140

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Arg Ile Asn Arg Leu
145          150          155          160

Thr Gly Tyr Leu Arg Asn
      165

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&lt;210&gt; 37

&lt;211&gt; 166

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 37

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Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
 1           5           10           15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
      20           25           30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
      35           40           45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
      50           55           60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
65           70           75           80

Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
      85           90           95

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Ile Ala Ala Tyr Leu Ala Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
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Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Arg Ile Asn Arg Leu  
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Thr Gly Tyr Leu Arg Asn  
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Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
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 20 25 30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
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Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
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Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
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Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
 85 90 95

His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
 100 105 110

Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
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Ile Leu His Tyr Leu Lys Ala Ala Ala Tyr Ser His Cys Ala Trp Thr  
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Thr Gly Tyr Leu Arg Asn  
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<210> 39

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&lt;400&gt; 39

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 1           5           10           15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
 20           25           30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
 35           40           45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
 50           55           60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
 65           70           75           80

Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
 85           90           95

His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
100          105          110

Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
115          120          125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ala Ala Cys Ala Trp Thr
130          135          140

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Arg Ile Asn Arg Leu
145          150          155          160

Thr Gly Tyr Leu Arg Asn
          165

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&lt;210&gt; 40

&lt;211&gt; 166

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 40

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Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
 1           5           10           15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
 20           25           30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
 35           40           45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
 50           55           60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
 65           70           75           80

Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
 85           90           95

His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
100          105          110

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Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
 130 135 140

Ile Val Arg Ala Glu Ile Leu Ala Asn Phe Ala Arg Ile Ala Arg Leu  
 145 150 155 160

Thr Gly Tyr Leu Arg Asn  
 165

<210> 41  
 <211> 166  
 <212> PRT  
 <213> Homo sapiens

<400> 41  
 Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
 1 5 10 15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
 20 25 30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
 35 40 45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
 50 55 60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
 65 70 75 80

Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
 85 90 95

His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
 100 105 110

Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
 130 135 140

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
 145 150 155 160

Thr Gly Tyr Leu Arg Asn  
 165

<210> 42  
 <211> 166  
 <212> PRT  
 <213> Homo sapiens

<400> 42  
 Met Ala Tyr Ala Ala Leu Gly Ala Leu Gln Ala Ser Ser Asn Phe Gln  
 1 5 10 15



Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
                   20                  25                  30  
 Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
                   35                  40                  45  
 Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
                   50                  55                  60  
 Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
   65                  70                  75                  80  
 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
                   85                  90                  95  
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
                   100                  105                  110  
 Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
                   115                  120                  125  
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
                   130                  135                  140  
 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
   145                  150                  155                  160  
 Thr Gly Tyr Leu Arg Asn  
                   165

<210> 43  
 <211> 166  
 <212> PRT  
 <213> Homo sapiens

<400> 43  
 Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Ala Ala  
   1                  5                  10                  15  
 Cys Ala Ala Leu Leu Ala Ala Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
                   20                  25                  30  
 Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
                   35                  40                  45  
 Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
                   50                  55                  60  
 Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
   65                  70                  75                  80  
 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
                   85                  90                  95  
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
                   100                  105                  110  
 Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
                   115                  120                  125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
 130 135 140

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
 145 150 155 160

Thr Gly Tyr Leu Arg Asn  
 165

<210> 44

<211> 166

<212> PRT

<213> Homo sapiens

<400> 44

Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
 1 5 10 15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Ala Ala Ala Cys Ala  
 20 25 30

Ala Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
 35 40 45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
 50 55 60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
 65 70 75 80

Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
 85 90 95

His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
 100 105 110

Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
 130 135 140

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
 145 150 155 160

Thr Gly Tyr Leu Arg Asn  
 165

<210> 45

<211> 166

<212> PRT

<213> Homo sapiens

<400> 45

Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
 1 5 10 15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
 20 25 30

Lys	Asp	Arg	Ala	Ala	Phe	Ala	Ile	Pro	Ala	Glu	Ile	Lys	Gln	Leu	Gln
35						40						45			
Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln
50						55				60					
Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp	Asn
65				70						75				80	
Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn
				85				90						95	
His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Asp	Phe	Thr
		100						105				110			
Arg	Gly	Lys	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg
		115				120						125			
Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp	Thr
130						135				140					
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Phe	Ile	Asn	Arg	Leu
145				150						155				160	
Thr	Gly	Tyr	Leu	Arg	Asn										
				165											

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<210> 46
<211> 166
<212> PRT
<213> Homo sapiens
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<400>	46															
Met	Ser	Tyr	Asn	Leu	Leu	Gly	Phe	Leu	Gln	Arg	Ser	Ser	Asn	Phe	Gln	
1				5					10					15		
Cys	Gln	Lys	Leu	Leu	Trp	Gln	Leu	Asn	Gly	Arg	Leu	Glu	Tyr	Cys	Leu	
			20					25					30			
Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile	Ala	Ala	Ala	Ala	
			35				40					45				
Ala	Phe	Ala	Ala	Ala	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln	
	50					55					60					
Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp	Asn	
65					70					75					80	
Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn	
				85					90					95		
His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Asp	Phe	Thr	
			100					105					110			
Arg	Gly	Lys	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg	
		115					120					125				

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
 130 135 140

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
 145 150 155 160

Thr Gly Tyr Leu Arg Asn  
 165

<210> 47

<211> 166

<212> PRT

<213> Homo sapiens

<400> 47

Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
 1 5 10 15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
 20 25 30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
 35 40 45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Ala  
 50 55 60

Asn Ile Ala Ser Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
 65 70 75 80

Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
 85 90 95

His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
 100 105 110

Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
 130 135 140

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
 145 150 155 160

Thr Gly Tyr Leu Arg Asn  
 165

<210> 48

<211> 166

<212> PRT

<213> Homo sapiens

<400> 48

Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
 1 5 10 15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
 20 25 30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
 35 40 45  
 Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
 50 55 60  
 Asn Ile Phe Ala Ile Phe Ala Ala Ala Ser Ser Ser Thr Gly Trp Asn  
 65 70 75 80  
 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
 85 90 95  
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
 100 105 110  
 Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125  
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
 130 135 140  
 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
 145 150 155 160  
 Thr Gly Tyr Leu Arg Asn  
 165

<210> 49  
 <211> 166  
 <212> PRT  
 <213> Homo sapiens

<400> 49  
 Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
 1 5 10 15  
 Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
 20 25 30  
 Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
 35 40 45  
 Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
 50 55 60  
 Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
 65 70 75 80  
 Ala Ser Ile Val Ala Ala Leu Leu Ser Asn Val Tyr His Gln Ile Asn  
 85 90 95  
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
 100 105 110  
 Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125  
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
 130 135 140

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
 145 150 155 160

Thr Gly Tyr Leu Arg Asn  
 165

<210> 50  
 <211> 166  
 <212> PRT  
 <213> Homo sapiens

<400> 50  
 Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
 1 5 10 15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
 20 25 30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
 35 40 45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
 50 55 60

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
 65 70 75 80

Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Ala His Gln Ile Ala  
 85 90 95

His Leu Ala Ala Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
 100 105 110

Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
 130 135 140

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
 145 150 155 160

Thr Gly Tyr Leu Arg Asn  
 165

<210> 51  
 <211> 166  
 <212> PRT  
 <213> Homo sapiens

<400> 51  
 Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
 1 5 10 15

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
 20 25 30

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
 35 40 45

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
 50 55 60  
 Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
 65 70 75 80  
 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
 85 90 95  
 His Leu Lys Thr Val Leu Ala Ala Lys Leu Ala Ala Ala Asp Phe Thr  
 100 105 110  
 Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125  
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
 130 135 140  
 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
 145 150 155 160  
 Thr Gly Tyr Leu Arg Asn  
 165

<210> 52  
 <211> 166  
 <212> PRT  
 <213> Homo sapiens

<400> 52  
 Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
 1 5 10 15  
 Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
 20 25 30  
 Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
 35 40 45  
 Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
 50 55 60  
 Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
 65 70 75 80  
 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
 85 90 95  
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Ala Ala Thr  
 100 105 110  
 Ala Gly Lys Ala Met Ser Ala Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125  
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
 130 135 140  
 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
 145 150 155 160

Thr Gly Tyr Leu Arg Asn  
165

<210> 53  
<211> 166  
<212> PRT  
<213> Homo sapiens

<400> 53  
Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
1 5 10 15  
Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
20 25 30  
Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
35 40 45  
Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
50 55 60  
Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
65 70 75 80  
Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
85 90 95  
His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
100 105 110  
Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Ala  
115 120 125  
Ile Ala Ala Tyr Leu Ala Ala Lys Glu Tyr Ser His Cys Ala Trp Thr  
130 135 140  
Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
145 150 155 160  
Thr Gly Tyr Leu Arg Asn  
165

<210> 54  
<211> 166  
<212> PRT  
<213> Homo sapiens

<400> 54  
Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
1 5 10 15  
Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
20 25 30  
Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
35 40 45  
Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
50 55 60



Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
 65 70 75 80  
 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
 85 90 95  
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
 100 105 110  
 Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125  
 Ile Leu His Tyr Leu Lys Ala Ala Ala Tyr Ser His Cys Ala Trp Thr  
 130 135 140  
 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
 145 150 155 160  
 Thr Gly Tyr Leu Arg Asn  
 165

<210> 55  
 <211> 166  
 <212> PRT  
 <213> Homo sapiens

<400> 55  
 Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln  
 1 5 10 15  
 Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu  
 20 25 30  
 Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln  
 35 40 45  
 Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln  
 50 55 60  
 Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn  
 65 70 75 80  
 Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn  
 85 90 95  
 His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr  
 100 105 110  
 Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg  
 115 120 125  
 Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ala Ala Cys Ala Trp Thr  
 130 135 140  
 Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu  
 145 150 155 160  
 Thr Gly Tyr Leu Arg Asn  
 165

<400> 56

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